

The Impact of Healthy Lifestyle Factors on Life Expectancies in the US population

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ABSTRACT

Background: Americans have a shorter life expectancy compared to almost all other high-income countries. We aim to estimate the impact of lifestyle factors on premature mortality and life expectancy in the US population.

Methods: Based on the Nurses' Health Study (1980-2014, n=78,865) and the Health Professionals Follow-up Study (1986-2014, n=44,354), we defined five low-risk lifestyle factors as fulfilling either: never smoking, body mass index (BMI) 18.5-24.9 kg/m², 30+ minutes/day moderate to vigorous physical activity, moderate alcohol intake, and a high diet quality score (upper 40%) and estimated hazard ratios (HRs) for the association of total lifestyle score (0-5 scale) with mortality. We used data from the NHANES (2013-2014) to estimate the distribution of the lifestyle score, and the US CDC WONDER database to derive the age-specific death rates of Americans. We applied life table method to estimate life expectancy by levels of the lifestyle score.

Results: During up to 34 years of follow-up, we documented 42,167 deaths. The multivariable-adjusted HRs for mortality in adults with five compared with zero low-risk factors were 0.26 (95% confidence interval [CI]: 0.22-0.31) for all-cause mortality, 0.35 (95% CI: 0.27-0.45) for cancer mortality and 0.18 (95% CI: 0.12-0.26) for CVD mortality. The population-attributable-risk of non-adherence to five low-risk factors was 60.7% (95% CI: 53.6%-66.7%) for all-cause mortality, 51.7% (95% CI: 37.1%-62.9%) for cancer mortality and 71.7% (58.1%-81.0%) for CVD mortality. We estimated that the life expectancy at age 50 was 29.0 years (95% CI: 28.3-29.8) for females and 25.5 years (95% CI: 24.7-26.2) for males who adopted zero low-risk lifestyle factors. In contrast, for those who adopted all five low-risk factors, we projected a life expectancy at age 50 of 43.1 years (95% CI: 41.3-44.9) for females and 37.6 years (95% CI:

35.8-39.4) for males. The projected life expectancy at age 50 was on average 14.0 (95% CI: 11.8-16.2) years longer among female Americans with five low-risk factors as compared to those with zero low-risk factors; for males, the difference was 12.2 (95% CI: 10.1-14.2) years.

Conclusion: Adopting a healthy lifestyle could substantially reduce premature mortality and prolong life expectancy in US adults.

KEYWORDS: healthy lifestyle, life expectancy, premature death

58 CLINICAL PERSPECTIVE

59 What is new?

- 60 • A comprehensive analysis of the impact of adopting low-risk lifestyle factors on life
61 expectancy in the US population is lacking.
- 62 • Adherence to five low-risk lifestyle-related factors (never smoking, a healthy weight,
63 regular physical activity, a healthy diet, and moderate alcohol consumption) could
64 prolong life expectancy at age 50 by 14.0 and 12.2 years for female and male US adults,
65 compared to individuals who adopted zero low-risk lifestyle factor.

66 What is the clinical implication?

- 67 • Americans could narrow the life-expectancy gap between the US and other industrialized
68 countries by adopting a healthier lifestyle.
- 69 • Prevention should be a top priority for national health policy and preventive care should
70 be an indispensable part of the US health care system.

INTRODUCTION

The United States (US) is one of the wealthiest nations worldwide, but Americans have a shorter life expectancy compared to almost all other high-income countries,^{1,2} ranking 53rd in the world for life expectancy at birth in 2015.³ In 2014, with a total health expenditure per capita of \$9,402,⁴ the US was ranked first in the world for health expenditure as a percent of GDP (17.1%).⁴ However, the US health care system has primarily focused on drug discoveries and disease treatment, rather than prevention. Chronic diseases, such as cardiovascular disease (CVD) and cancer, are the most common and costly of all health problems, but are largely preventable.⁵ It has been widely acknowledged that unhealthy lifestyles are major risk factors for various chronic diseases and premature death.⁶

More than two decades ago, McGinnis et al. suggested that the nation's major health policies should move to emphasize reducing unhealthy lifestyles.^{7,8} A meta-analysis⁹ of 15 studies including 531,804 participants from 17 countries with a mean follow-up of 13.24 years, suggested that approximately 60 percent of premature deaths could be attributed to unhealthy lifestyle factors, including smoking, excessive alcohol consumption, physical inactivity, poor diet, and obesity. A healthy lifestyle was associated with an estimated increase of 7.4-17.9 years in life expectancy in Japan,¹⁰ the UK,¹¹ Canada,¹² Denmark,¹³ Norway¹³ and Germany.^{13,14} However, a comprehensive analysis of the impact of adopting low-risk lifestyle factors on life expectancy in the US population is lacking. Therefore, we aimed to evaluate the potential impact of individual and combined lifestyle factors on premature death and life expectancy in the US population.

METHODS

Disclosure Statement

The data, analytic methods, and study materials will be made available to other researchers from the corresponding author upon reasonable request for purposes of reproducing the results or replicating the procedure.

Overall Design

We first quantified the association between lifestyle-related low-risk factors and mortality based on cohort data from the Nurses' Health Study (NHS)^{15,16} and the Health Professionals Follow-up Study (HPFS).¹⁷ Then, we used data from the NHANES (2013-2014) to estimate the distribution of the lifestyle-related factors among the US population.¹⁸ Furthermore, we derived the death rates of Americans from the CDC WONDER database.¹⁹ Finally, we combined the results from those three sources to estimate the extended life expectancy associated with different categories of each individual lifestyle factor and a combination of low-risk lifestyle factors.

Study Population

The NHS began in 1976, when 121,700 female nurses aged 30 to 55 years responded to a questionnaire gathering medical, lifestyle, and other health-related information. In 1980, 92,468 nurses also responded to a validated food frequency questionnaire (FFQ)^{15,16}. The HPFS¹⁷ was established in 1986, when 51,529 male US health professionals (dentists, optometrists, osteopaths, podiatrists, pharmacists, and veterinarians) aged 40–75 years completed a mailed questionnaire about their medical history and lifestyle, including a FFQ. We excluded participants with implausible energy intakes (female: <500 or >3500 kcal/day; male: <800 or >4200 kcal/day), a Body Mass Index (BMI) <18.5 kg/m² at baseline, or with a missing value for BMI, physical activity, alcohol or smoking. After these exclusions, 78,865 female and 44,354 male participants remained in the analysis at baseline. The NHS and HPFS were approved by the

institutional review board of Brigham and Women's Hospital in Boston; completion of the self-administered questionnaire was considered to imply informed consent.

We used the NHANES (2013-2014)¹⁸ to estimate the population distribution of lifestyle related factors among American adults. The analytic population consisted of 2,128 adults aged 50 to 80 years with complete information on diet, BMI, physical activity, alcohol use and smoking status. We also excluded participants with BMIs of less than 18.5 kg/m². The NHANES¹⁸ included a nationally representative sample of the US population. It was approved by the National Center for Health Statistics research ethics review board. Signed consents were obtained from all participants.

Data Collection

Diet in the NHS and HPFS was assessed every 4 years using a validated FFQ asking the frequency, on average, a participant had consumed a particular amount of a specific type of food during the previous year.^{15,16} Physical activity levels were investigated using a validated questionnaire and updated every 2 years.²⁰ Body weight and smoking habits were self-reported and updated every two years. Alcohol consumption was also collected by the FFQ. Biennial questionnaires were used to collect information on potential confounders, such as age, ethnicity, multi-vitamin use, regular aspirin use, postmenopausal hormone use (NHS only), and the presence or absence of a family history of diabetes, cancer, or myocardial infarction.

Dietary data in the NHANES¹⁸ were collected by an interviewer-administered, computer-assisted, 24-hour dietary recall, which was an in-depth interview conducted by a trained interviewer who solicited detailed information about everything that the participant ate and drank in the prior twenty-four hours. Body weight and height were measured in a mobile examination center using standardized techniques and equipment. Smoking status was self-reported and

included questions about numbers of cigarettes, pipes, or cigars smoked per day, and whether the participant had smoked at least 100 cigarettes in his or her lifetime. Participants also reported duration of moderate and vigorous physical activity during leisure time and at work. Usual alcohol intakes were recorded by two 24-hour dietary recalls.¹⁸

Low-risk Lifestyle Score

We included five lifestyle-related factors—diet, smoking, physical activity, alcohol consumption, and BMI. Because this study was focused on modifiable lifestyle factors, we did not include clinical risk factors such as hypertension, hypercholesterolemia, or medication use in the score.

Diet quality in the NHS, HPFS and NHANES was assessed using the Alternate Healthy Eating Index (AHEI) score (**eMethod**) that is strongly associated with the onset of cardiometabolic disease in the general population.²¹⁻²³ We defined a healthy diet as a diet score in the top 40% of each cohort distribution. For smoking, we defined low-risk as never smoking. For physical activity, we classified low-risk as more than 30 minutes a day of moderate or vigorous activities (including brisk walking) that require the expenditure of at least 3 metabolic equivalents (METs) or more per hour. We defined low-risk alcohol consumption as moderate alcohol consumption, e.g. 5-15 g/day for females and 5-30 g/day for males. BMI was calculated as self-reported weight (kg)/height (m)². Low-risk body weight was defined as BMI in the range of 18.5-24.9 kg/m².

For each low-risk factor, the participant received a score of 1 if he or she met the criterion for low-risk. If the participant did not meet the criterion, he or she was classified as high-risk for that factor and received a score of 0. The sum of these five scores provided a total number of low-risk factors of 0, 1, 2, 3, 4 or 5 with higher scores indicating a healthier lifestyle.

Ascertainment of Deaths

In the NHS and HPFS, deaths were identified from state vital statistics records, the National Death Index, reports by the families, and the postal system.²⁴ The follow-up for death in both cohorts was at least 98% complete. A physician reviewed death certificates or medical records to classify the cause of death according to ICD-8 in the NHS (ICD-9 in the HPFS).

We also derived the population all-cause, cardiovascular (I00-I99) and cancer mortality (C00-D48) rates for 2014 by gender and single-year ages ranging from 50 to 84 years from the CDC WONDER database of the US population.¹⁹ Because the database only provides mortality rates up to age 84 years, we estimated the all-cause and cause-specific mortality rates in single years of age from 85 to 105 years by extrapolation based on a Poisson regression model with both linear and quadratic terms for the midpoints of single-year age groups minus age 50.5 years (eMethod, eFigure 1).

Statistical Analysis

Participants contributed person time from the return of the baseline questionnaire (NHS, 1980; HPFS, 1986) until the date of death, or the end of the follow-up period (30 June 2014 for NHS and 30 January 2014 for HPFS), whichever came first. We used Cox proportional hazard models to calculate the adjusted hazard ratios (HRs) of all-cause, cancer and cardiovascular mortality with their 95% confidence intervals (CIs) across categories of each individual factor and joint classification of number of low-risk factors (0, 1, 2, 3, 4 or 5).

Because lifestyle factors may affect mortality risk over an extended period of time, to best represent long-term effects, we calculated cumulative average levels of lifestyle factors using the latest two repeated measurements for our primary analysis of diet, physical activity and alcohol consumption. For example, in the NHS, mortality cases that occurred between 1980 and 1982

were examined in relation to physical activity based on data collected on the 1980 questionnaire; the average of 1980 and 1982 physical activity measurements was used to assess risk of mortality in the 1982–1984 follow-up period, the average of 1982 and 1984 physical activity measurements was used to assess risk of mortality in the 1984–1986 follow-up period, and so forth. For dietary AHEI score and alcohol, the average was calculated based on four-year repeated measurements. Smoking status was estimated based on both smoking history and most recent status updated every other year and classified into five categories: never, past, current smoking of 1-14, 15-24 and ≥ 25 cigarettes/day. To minimize the reverse causality bias resulting from weight loss due to preexisting illness, we applied the lifelong maximum BMI²⁵. For example, we applied the maximum value of BMI at age 18 and BMI in 1980 to predict mortality between 1980 and 1982, and the maximum value of BMI at age 18, BMI in 1980 and BMI in 1982 to predict mortality between 1982 and 1984, and so forth. The same analytic strategy was applied to the HPFS. If data on low-risk factors were missing at a given time point, the last observation was carried forward. The following covariates were included in the multivariable model: age, ethnicity, current multivitamin use, current aspirin use, menopausal status and hormone use (females only), and family history of diabetes, myocardial infarction, or cancer. We applied competing risk regression model for cause-specific mortality by including lifestyle factors as exposure and other risk factors as unconstrained covariates, allowing the effects of the covariates vary across cause-specific mortality.²⁶

We calculated the hypothetical population-attributable-risk (PAR), an estimation of the percentage of premature mortality in the study population that theoretically would not have occurred if all people had been in the low-risk category, assuming that the observed associations represent causal effects. For these analyses, we used a single binary categorical variable (with all

5 low-risk factors) and compared participants in the low-risk category with the rest of the population (without all 5 low-risk factors or with any high-risk factor) to calculate the HR. We combined these HRs with the prevalence of the low-risk category among American adults based on NHANES data to estimate the PAR.²⁷

To calculate the life expectancy of participants following different levels of healthy lifestyles, we used life tables. We built the life table starting at age 50 years and ending at 105 years with the following three estimates to calculate the cumulative survival from 50 years onward: (1) Sex- and age- specific HRs of mortality associated with numbers of low-risk lifestyles, derived from the NHS and HPFS; (2) sex- and age-specific population mortality rate of all causes, cardiovascular mortality (I00-I99) and cancer mortality (C00-D48) from the US CDC WONDER database;¹⁹ (3) age- and sex-specific population prevalence of the number of low-risk lifestyles, derived from the NHANES.¹⁸ We fitted multivariable-adjusted Cox regression models for each gender separately to calculate the age specific hazard ratios for mortality by the number of low-risk factors as compared with zero low-risk factors. The model specification included linear and quadratic terms for the age variable (every 5-years, up to 85 years), and the interactions between the number of low-risk factors with linear and quadratic terms of age variable. The age specific hazard ratios for mortality were obtained as linear combinations of the relevant estimated coefficients, with age fixed at values corresponding to midpoints of 5-year age-group from age 50 onwards to age 85. The HR of age above 85 was assumed to be the same as that in the 85 years age group. Then we applied the age- and sex-specific HRs to estimate the life expectancy at different ages by the number of low-risk lifestyle factors (**eMethod**).

In the sensitivity analysis, we applied the sex-specific HRs (adjusted for age only) for all-cause and cause-specific mortality to test the robustness of our findings. To address the potential aging effect on the association between lifestyle and mortality, we conducted a sensitivity analysis limited to NHS and HPFS participants prior to age 75 years. We conducted three stratified analyses, one stratified by smoking status, another stratified by BMI status, to estimate the joint effect of other four lifestyle factors; the third was stratified by baseline disease status (with or without elevated cholesterol, hypertension or diabetes). To address the concern about the potential adverse effects of moderate alcohol intake, we created a healthy lifestyle score based on the other four low-risk factors without alcohol.

Since the binary variables could not account for the gradient in mortality risk with more extreme levels of these lifestyle factors, we conducted a third sensitivity analysis, in which we calculated an expanded low-risk score based on the associations between each lifestyle factor and mortality in the cohorts. We assigned scores of 1 (least healthy) to 5 (most healthy) to the categories of the lifestyle factors and summed the points across all 5 factors (score range, 5-25 points). For this analysis, the healthiest group was defined as never smoking, BMI between 18.5 and 22.9, moderate alcohol intake (5-14.9 g/day), moderate or vigorous activity duration of 6 hours/week or longer, and the highest quintile of the AHEI diet score.

We used SAS version 9.3 (SAS Institute Inc., Cary, NC, USA) to analyze the data. Statistical significance was set at a two-tailed P value <0.05. We used Monte Carlo simulation (parametric bootstrapping) with 10,000 runs to calculate the confidence intervals of the life expectancy estimation with @RISK 7.5 (Palisade Corporation, Ithaca, NY, USA).

RESULTS

At baseline, participants with a higher number of low-risk lifestyle factors were slightly younger, more likely to use aspirin, and less likely to use multivitamin supplements (**Table 1**). During a median of 33.9 years follow-up of females and 27.2 years follow-up of males, 42,167 deaths were recorded (13,953 deaths from cancer and 10,689 deaths from CVD).

Each individual component of a healthy lifestyle showed a significant association with risk of total mortality, cancer mortality and CVD mortality (**Table 2**). A combination of five low-risk lifestyle factors was associated with a HR (95% CI) of 0.26 (0.22-0.31) for all-cause mortality, 0.35 (0.27-0.465) for cancer mortality and 0.18 (0.12-0.26) for CVD mortality as compared with participants with zero low-risk factors. The PAR (95% CI) of non-adherence to 5 low-risk lifestyle factors was 60.7% (53.6%-66.7%) for all-cause mortality, 51.7% (37.1%-62.9%) for cancer mortality, and 71.7% (58.1%-81.0%) for cardiovascular mortality. We observed a similar association between the low-risk lifestyle factors and mortality prior to 75 years (**eTable 1**). The low-risk lifestyle factors were associated with lower risk of cause-specific mortality in females and males similarly (**eFigure 2**).

We observed a modest difference in HRs across age groups (**Figure 1A**). Using these age- and sex-specific HRs, we estimated that the life expectancy at age 50 was 29.0 years (95% CI: 28.3-29.8) for females and 25.5 years (95% CI: 24.7-26.2) for males who adopted zero low-risk lifestyle factors. In contrast, for those who adopted all five low-risk factors, we projected a life expectancy at age 50 of 43.1 years (95% CI: 41.3-44.9) for females and 37.6 years (95% CI: 35.8-39.4) for males (**Figure 1B**). Equivalently, females with five low-risk lifestyle factors could gain 14.0 (95% CI: 11.8-16.8) years of life expectancy on average, and males could gain 12.2 (95% CI: 10.1-14.2) years of life expectancy compared to those with zero low-risk lifestyle factors (**Figure 1C**). The preceding inferences were similar in sensitivity analyses using sex-

specific HRs adjusted for age only (**eFigure 3A and 3B**). Among females, on average, about 30.8% of the gained life expectancy at age 50 from adopting five versus zero low-risk lifestyle factors was attributable to reduced CVD death, and the remainder to lower cancer (21.2%) or other causes (48.0%) of mortality, respectively. For males, the corresponding percentage was 34.1%, 22.8% and 43.1%, respectively (**eFigure 3C**). We observed a consistent dose-response relationship between the increasing number of low-risk factors and gained life expectancy among both smokers and non-smokers (**eFigure 4**), among both normal weight and overweight adults (**eFigure 5**) and among individuals with and without chronic conditions at baseline (**eFigure 6**).

In a sensitivity analysis using a low-risk score without moderate alcohol intake, the projected life expectancy at age 50 was on average 11.4 (95% CI: 9.5-13.3) years longer among female Americans with four low-risk factors as compared to those with zero low-risk factors; for males, the difference was 10.0 (95% CI: 9.2-10.9) years (**eFigure 7**).

We also estimated the gained life expectancy related to each of the lifestyle factors. As expected, increased exercise, not smoking or a reduced amount of smoking if a smoker, a healthy dietary pattern, moderate alcohol intake, and optimal body weight were all associated with longer life expectancy (**Figure 2**). The estimate based on the expanded low-risk score indicated a maximum of 20.5 years difference in life expectancy at age 50 in females (19.6 years among males) who adhered to the highest expanded lifestyle score compared to the lowest expanded score (**eFigure 8**).

DISCUSSION

We estimated that adherence to five low-risk lifestyle-related factors could prolong life expectancy at age 50 by 14.0 and 12.2 years for female and male US adults, compared to individuals who adopted zero low-risk lifestyle factor. These estimates suggest that Americans

could narrow the life-expectancy gap between the US and other industrialized countries by adopting a healthier lifestyle. In 2014, the life expectancy for American adults at age 50 was 33.3 years for females and 29.8 years for males.²⁸ We estimated that the life expectancies were 29.0 years for females and 25.5 years for males if they had zero low-risk factors, but could be extended to 43.1 years for females and 37.6 years for males if they adopted all five low-risk factors. However, in US adults, adherence to a low-risk lifestyle pattern has decreased during the last three decades, from 15% in 1988-1992 to 8% in 2001-2006,²⁹ primarily driven by the increasing prevalence of obesity.

The life expectancy of Americans increased from 62.9 years in 1940 to 76.8 in 2000 and 78.8 in 2014.²⁸ This increase could be due to a number of factors, such as improvements in living standards, improved medical treatment, substantial reduction in smoking³⁰ and a modest improvement in diet quality.²³ However, some unhealthy lifestyle factors may have counterbalanced the gain in life expectancy, particularly the increasing obesity epidemic^{30,31} and decreasing physical activity levels.³² In our study, three fourths of premature CVD deaths and half of premature cancer deaths in the U. S. could be attributed to lack of adherence to a low-risk lifestyle. There is still much potential for improvement in health and life expectancy, which depends not only on an individual's efforts, but also the food, physical, and policy environments.^{33,34} A recent study found that low-income residents in relatively wealthy areas, such as New York and San Francisco, had significantly longer life expectancies than those in poorer regions, such as Gary, Indiana, and Detroit, Michigan.³⁵ This phenomenon suggests that the living environment contributes to life expectancy beyond socio-economic status. For instance, the residents in affluent cities have more access to public health services and less exposure to smoking due to the more restricted policies regarding smoking in public.³⁵ Studies³⁶ have linked

healthy eating and exercise habits with built, social, and socioeconomic environment assets (access to parks, social ties, affluence), and unhealthy behaviors with built environment inhibitors (access to fast food outlets), suggesting that supporting environments for health lifestyle should be one part of the promotion of longevity for U.S. population. Prevention should be a top priority for national health policy and preventive care should be an indispensable part of the health care system.

Our estimation of gained life expectancy by adopting a low-risk lifestyle was broadly consistent with previous studies. A healthy lifestyle was associated with an estimated greater life expectancy of 8.3 (females) and 10.3 (males) years in Japan,¹⁰ 17.9 years in Canada,¹² 13.9 years (females) and 17.0 years (males) in Germany,¹⁴ and 14 years difference in chronological age in the UK.¹¹ Data from three European cohorts from Denmark, Germany and Norway¹³ suggested that males and females aged 50 years who had a favorable lifestyle would live 7.4 -15.7 years longer than those with an unfavorable lifestyle. These estimates were somewhat different, because of different definitions of a low-risk lifestyle and study population characteristics.^{10,12-14}

We observed that adherence to a healthy diet pattern, moderate alcohol consumption, nonsmoking status, maintaining a normal weight and regular physical activity was each associated with a low risk of premature mortality. Smoking is a strong independent risk factor of cancer, diabetes, cardiovascular diseases and mortality potentially through inducing oxidative stress and chronic inflammation; and smoking cessation has been associated with a reduction of these excess risks.³⁷⁻³⁹ A healthy dietary pattern and its major food components have been associated with lower risk of morbidities and mortality of diabetes, cardiovascular disease, cancer and neurodegenerative disease;⁴⁰ and its potential health benefits have been replicated in clinical trials.⁴¹ Physical activity and weight control significantly reduced the risk of diabetes,

cardiovascular risk factors and breast cancer.⁴²⁻⁴⁴ Although no long-term trial of alcohol consumption on chronic disease risk has been conducted, cardiovascular benefits of moderate alcohol consumption have been consistently observed in large cohort studies.⁴⁵ Results of our sensitivity analysis further indicated that combinations of the healthy lifestyle factors were particularly powerful; the larger the number of low-risk lifestyle factors, the longer was the potential prolonged life expectancy, regardless of the combined factors.⁴⁶

A major strength of this study is the long follow-up of two large cohorts with detailed and repeated measurements of diet and lifestyle and low rates of loss to follow-up. Another important strength is the combination of the cohort estimates with a nationally representative study, the NHANES, which improved the generalizability of our findings. Although the hazard ratios between lifestyle factors and mortality were estimated based only on our cohort data, they were similar to those published in other populations⁹⁻¹⁴. As our cohorts included mostly Caucasian health professionals, we could not specifically examine the overall impact of lifestyle adherence among different ethnic subgroups; further studies are warranted to examine the impact of lifestyle factors in other ethnic and racial groups.

The current study has several limitations. First, diet and lifestyle factors were self-reported and thus measurement errors are inevitable. However, the use of repeated measures of these variables could reduce measurement errors and also represent long-term diet and lifestyle. Second, we counted the number of lifestyle factors based on the dichotomized value of each lifestyle factor, although the lifestyle factors were differentially associated with mortality. However, our analysis based on an expanded score considered different levels of each risk factor, and yielded similar results. Third, we did not fully consider the baseline comorbid conditions and background medical therapies. Although our stratification analysis by baseline chronic

conditions of diabetes, hypertension and elevated cholesterol provided some support for the hypothesis that adopting a healthy lifestyle is important for both healthy individuals and those with existing chronic conditions, further studies among individuals with diagnosed cancer and cardiovascular diseases are warranted.

In conclusion, we estimate that adherence to a low-risk lifestyle could prolong life expectancy at age 50 by 14.0 and 12.2 years in female and male US adults compared to individuals without any of the low-risk lifestyle factors. Our findings suggest that the gap in life expectancy between the US and other developed countries could be narrowed by improving lifestyle factors.

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Conflict of Interest

The authors have no competing interests.

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ACCEPTED MANUSCRIPT

FIGURE LEGENDS

Figure 1: Life expectancy estimated based on overall mortality rate of Americans (CDC report), the prevalence of lifestyle factors using NHANES data 2013-2014 and age- and sex-specific hazard ratios*

* Low-risk lifestyle factors included: cigarette smoking (never smoking), physically active (≥ 3.5 hours/week moderate to vigorous intensity activity), high diet quality (upper 40% of alternative healthy eating index (AHEI), moderate alcohol intake of 5-15 g/day (female) or 5-30 g/day (male), and normal weight (body mass index $< 25 \text{ kg/m}^2$).

** The estimates of cumulative survival from 50 years of age onward among the 5 lifestyle risk factor groups were calculated by applying

^a All-cause and cause-specific mortality rates were obtained from the US CDC WONDER database;

^b Distribution of different numbers of low-risk lifestyles was based on the US NHANES 2013-2014;

^c Multivariate-adjusted hazard ratios (sex-and age-specific) for all-cause mortality associated with the 5 low-risk lifestyles as compared to those without any low-risk lifestyle factors, adjusted for ethnicity, current multivitamin use, current aspirin use, family history of diabetes mellitus, myocardial infarction, or cancer, and menopausal status and hormone use (females only), were based on data from the NHS and HPFS.

Figure 2: Projected gained or lost life expectancy according to individual low-risk lifestyle factors*

** The estimates of cumulative survival from 50 years of age onward among different levels of each lifestyle factor were calculated by applying

^a All cause and cause-specific mortality rate were obtained from the US CDC WONDER database;

^b Distributions of different groups of each lifestyle factor were based on the US NHANES 2013-2014;

^c Multivariate-adjusted hazard ratios (gender-specific) for all-cause and cause-specific mortality associated with each lifestyle factor adjusted for ethnicity, current multivitamin use, current aspirin use, family history of diabetes mellitus, myocardial infarction, or cancer, menopausal status and hormone use (females only), were based on data from the NHS and HPFS.

Table 1 Participant characteristics* at baseline according the number of low-risk lifestyle factors

	The number of low-risk lifestyle factors**					
	0	1	2	3	4	5
Nurses' Health Study (1980)						
N (%)	5216(7.1)	19200(26.3)	26790(36.7)	19563(26.8)	7179(9.8)	917(1.3)
Age, years	47.2(6.9)	46.7(7.1)	46.1(7.2)	45.8(7.3)	45.7(7.3)	45.7(7.3)
BMI, kg/m ²	29.8(4.5)	26.6(5.0)	24.5(4.1)	23.1(3.0)	22.3(1.9)	22.1(1.6)
Alternate Healthy Eating Index	26.7(3.4)	28.5(5.0)	30.6(6.0)	33.3(6.2)	35.9(5.5)	37.5(4.3)
Physical activity, hours/week	1.7(1.2)	2.4(2.1)	3.6(2.8)	5.1(2.9)	6.5(2.1)	7.1(1.2)
Alcohol consumption, gram/day	5.6(12.6)	6.2(12.4)	6.3(10.8)	6.5(9.1)	7.1(6.8)	9.5(2.8)
Past smoking, %	48.5	33.1	27.7	22.9	15.7	0.0
Current smoking, %	51.5	41.9	28.8	18.2	9.8	0.0
White, %	97.9	97.7	97.6	97.4	97.4	97.8
Multivitamin use, %	73.2	69.8	66.3	62.0	60.3	57.8
Regular aspirin use, %	49.4	51.9	53.2	53.5	55.6	52.5
Family history of diabetes, %	34.3	30.8	28.3	26.2	25.0	25.1
Family history of cancer, %	13.0	13.3	14.1	14.1	14.7	14.1
Family history of Myocardial Infarction, %	27.3	25.6	24.6	24.1	24.0	23.5
Health Professionals' Follow-up Study (1986)						
N (%)	4388(11.4)	12133(31.6)	14151(36.9)	9337(24.4)	3680(9.6)	665(1.7)
Age, years	55.0(9.6)	54.1(9.6)	53.6(9.8)	53.7(9.8)	53.2(9.9)	53.0(9.4)
BMI, kg/m ²	28.2(3.2)	27.1(3.4)	25.8(3.3)	24.7(2.8)	23.8(2.0)	23.2(1.2)
Alternate Healthy Eating Index	39.5(6.7)	42.9(9.5)	47.2(10.7)	51.6(10.4)	55.8(8.9)	58.6(6.8)
Physical activity, hours/week	0.7(0.9)	1.4(2.5)	2.5(3.6)	4.3(5.4)	6.2(5.4)	7.9(5.5)
Alcohol consumption, gram/day	16.3(23.7)	11.6(17.7)	10.3(13.7)	10.5(11.2)	10.7(8.7)	12.6(5.7)
Past smoking, %	76.6	54.2	41.9	30.2	18.1	0.0
Current smoking, %	23.4	14.9	7.8	3.3	1.5	0.0
White, %	94.5	94.2	93.8	94.0	94.5	97.0
Multivitamin use, %	43.0	41.3	38.8	35.9	31.6	33.1
Regular aspirin use, %	68.3	68.3	70.4	70.0	72.3	73.3
Family history of diabetes, %	22.1	22.9	20.9	19.9	19.9	21.8
Family history of cancer, %	32.5	33.1	34.4	35.1	35.2	37.1
Family history of Myocardial Infarction, %	34.4	33.7	33.3	34.0	32.6	33.6

*Values are means (SD) or percentages and are standardized to age distribution of the study population except age itself;

**Low-risk lifestyle factors included: cigarette smoking (never smoking), physically active (≥ 3.5 hours/week moderate to vigorous intensity activity), high diet quality (upper 40% of alternative healthy eating index (AHEI), moderate alcohol intake of 5-15 g/day (female) or 5-30 g/day (male), and normal weight (body mass index 18.5-24.9 kg/m²).

Table 2 Hazard ratios (95% CIs) of total and cause-specific mortality according to individual lifestyle risk factors*

	Person Years	<u>Deaths from any cause</u>		<u>Cancer deaths</u>		<u>Cardiovascular deaths</u>	
		Cases	RR (95% CI)	Cases	RR (95% CI)	Cases	RR (95% CI)
Body mass index (kg/m²)							
18.5-22.9	624140	5337	1.06 (1.02-1.09)	1868	0.96 (0.91-1.02)	1077	1.02 (0.94-1.10)
23-24.9	677848	7289	1.0(ref.)	2588	1.0(ref.)	1716	1.0(ref.)
25-29.9	1381081	17903	1.05 (1.02-1.08)	5935	1.01 (0.96-1.06)	4738	1.16 (1.10-1.23)
30-34.9	518621	7427	1.25 (1.21-1.29)	2371	1.12 (1.05-1.18)	2006	1.66 (1.56-1.78)
≥35	250013	4211	1.67 (1.61-1.74)	1191	1.24 (1.16-1.33)	1152	2.58 (2.39-2.79)
Cigarette smoking							
Never	1508401	13694	1.0(ref.)	4324	1.0(ref.)	3390	1.0(ref.)
Past	1505488	23155	1.41 (1.38-1.44)	7526	1.50 (1.44-1.56)	6045	1.38 (1.32-1.44)
Current 1-14/day	174422	2458	2.02 (1.93-2.10)	873	2.00 (1.86-2.15)	596	2.08 (1.91-2.27)
Current 15-24/day	163678	1756	2.33 (2.21-2.45)	729	2.28 (2.11-2.48)	428	2.62 (2.37-2.91)
Current ≥25/day	99716	1104	2.87 (2.70-3.06)	501	2.97 (2.70-3.27)	230	2.78 (2.43-3.19)
Alcohol consumption (g/day)							
0	1037840	16611	1.27 (1.24-1.30)	4671	1.03 (0.98-1.08)	4263	1.49 (1.41-1.57)
1-4.9	1087210	10454	1.03 (1.00-1.06)	3841	0.98 (0.93-1.03)	2632	1.13 (1.07-1.20)
5-14.9	773186	8041	1.0(ref.)	2953	1.0(ref.)	2007	1.0(ref.)
15-29.9	345034	4009	0.99 (0.96-1.03)	1417	0.99 (0.93-1.06)	1017	0.97 (0.90-1.05)
≥30	208434	3052	1.25 (1.19-1.30)	1071	1.21 (1.13-1.30)	770	1.17 (1.08-1.27)
Physical activity (hours/week)							
0	1089120	24254	1.0(ref.)	6997	1.0(ref.)	6177	1.0(ref.)
0.1-0.9	921192	8239	0.65 (0.63-0.66)	3044	0.71 (0.68-0.75)	2159	0.69 (0.66-0.73)
1.0-3.4	515731	3751	0.56 (0.54-0.58)	1491	0.66 (0.62-0.70)	930	0.54 (0.50-0.57)
3.5-5.9	369688	2524	0.50 (0.48-0.52)	1023	0.60 (0.56-0.64)	590	0.44 (0.40-0.48)
≥6	555972	3399	0.44 (0.43-0.46)	1398	0.55 (0.52-0.58)	833	0.39 (0.37-0.43)
Alternative healthy eating index							
Fifth 1	736051	11125	1.0(ref.)	3438	1.0(ref.)	2588	1.0(ref.)
Fifth 2	701947	9228	0.86 (0.83-0.88)	2983	0.89 (0.85-0.93)	2306	0.89 (0.84-0.94)
Fifth 3	689795	8082	0.77 (0.75-0.79)	2677	0.81 (0.77-0.85)	2073	0.81 (0.76-0.86)
Fifth 4	672973	7250	0.70 (0.68-0.72)	2511	0.76 (0.72-0.80)	1954	0.75 (0.71-0.80)
Fifth 5	650937	6482	0.63 (0.61-0.65)	2344	0.70 (0.67-0.74)	1768	0.67 (0.63-0.71)
Number of 5 low-risk factors**							
Zero	458169	9286	1.0(ref.)	2785	1.0(ref.)	2430	1.0(ref.)
One	1101853	16329	0.79 (0.77-0.81)	5227	0.83 (0.79-0.87)	4143	0.75 (0.71-0.79)
Two	1053250	10908	0.61 (0.59-0.62)	3821	0.68 (0.65-0.71)	2719	0.54 (0.51-0.57)
Three	596784	4408	0.47 (0.45-0.49)	1607	0.53 (0.50-0.57)	1101	0.40 (0.38-0.43)
Four	208683	1113	0.35 (0.33-0.37)	458	0.44 (0.40-0.49)	270	0.28 (0.25-0.32)
Five	32964	123	0.26 (0.22-0.31)	55	0.35 (0.27-0.45)	26	0.18 (0.12-0.26)
For not having five low-risk factors vs. all others (95% CI)		HRs	0.39 (0.33-0.46)		0.48 (0.37-0.63)		0.28 (0.19-0.42)
		PAR[§] (%)	60.7 (53.6-66.7)		51.7 (37.1-62.9)		71.7 (58.1-81.0)

HR: Hazard ratio; PAR: Population-Attributable-Risk

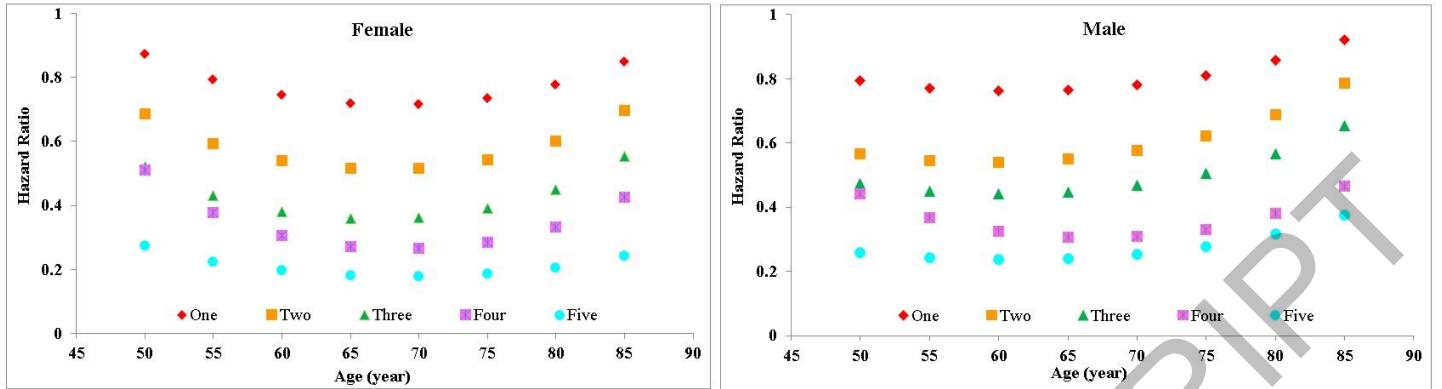
* Multivariable adjusted hazard ratio adjusted for age, sex, ethnicity, current multivitamin use, current aspirin use, family history of diabetes mellitus, myocardial infarction, or cancer, and, menopausal status and hormone use (females only).

** Low-risk lifestyle factors included: cigarette smoking (never smoking), physically active (≥3.5 hours/week moderate to vigorous intensity activity), high diet quality (upper 40% of alternative healthy eating index (AHEI), moderate alcohol intake of 5-15 g/day (female) or 5-30 g/day (male), and normal weight (body mass index 18.5-24.9 kg/m²).

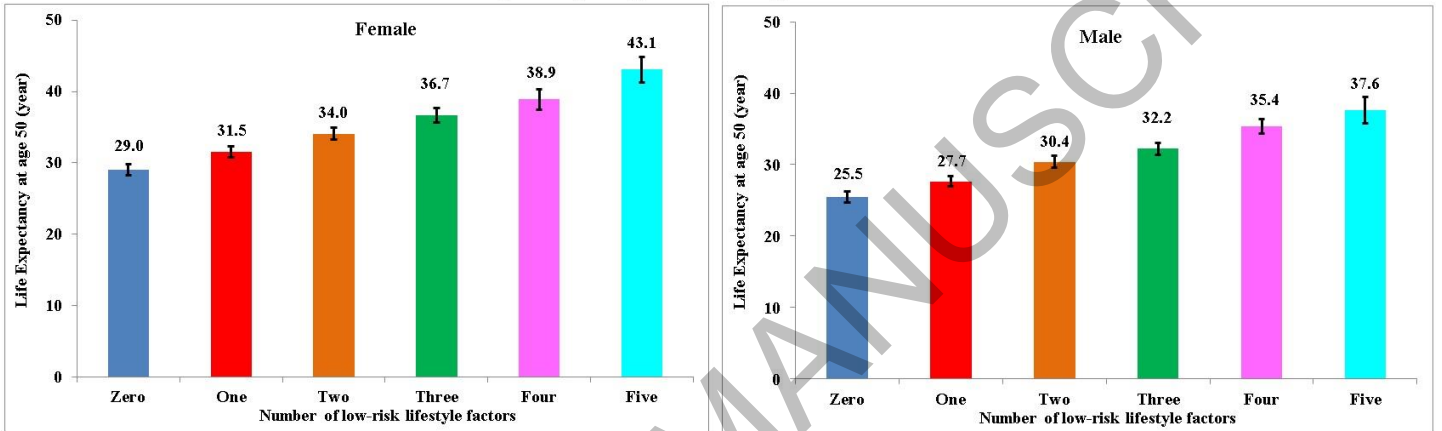
§ Estimation of PAR was based on the prevalence of not having five low-risk factors among American adults from NHANES data.

Figure 1

A: Age- and sex- specific hazard ratio for all-cause mortality by number of low-risk factors as compared with zero low-risk factor:



B: Estimated life expectancy at age 50 according to the number of low-risk factors



C. Gained life expectancy by applying healthy lifestyles as compared to none healthy lifestyle

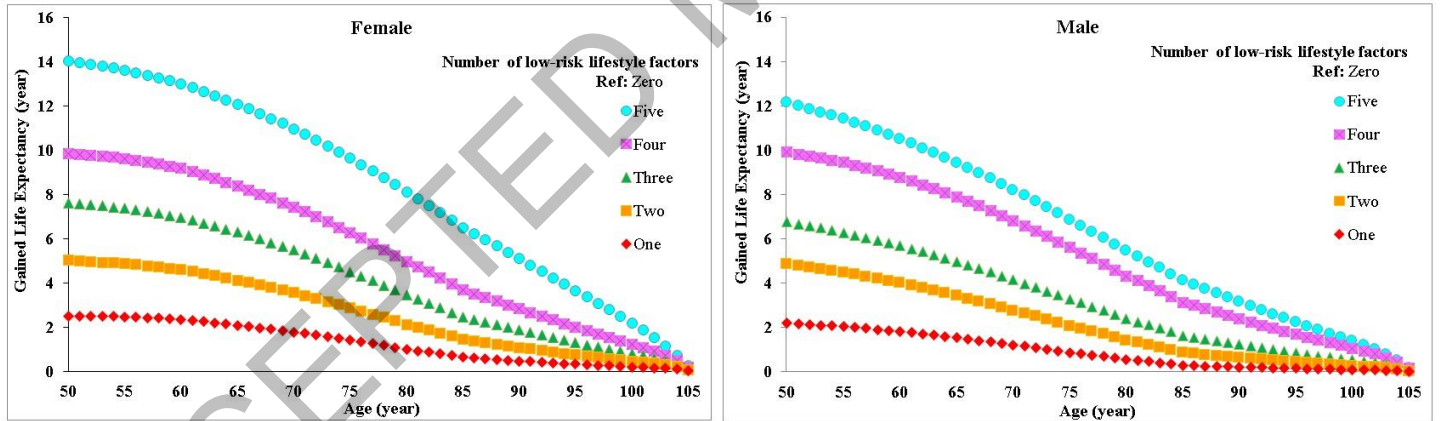
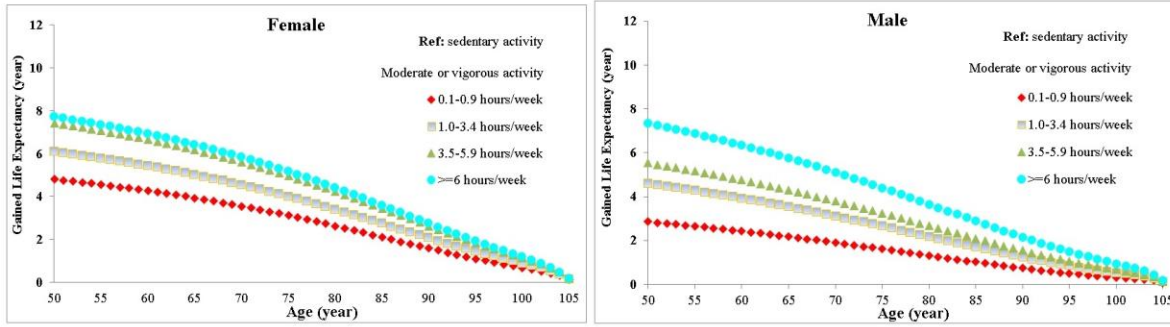
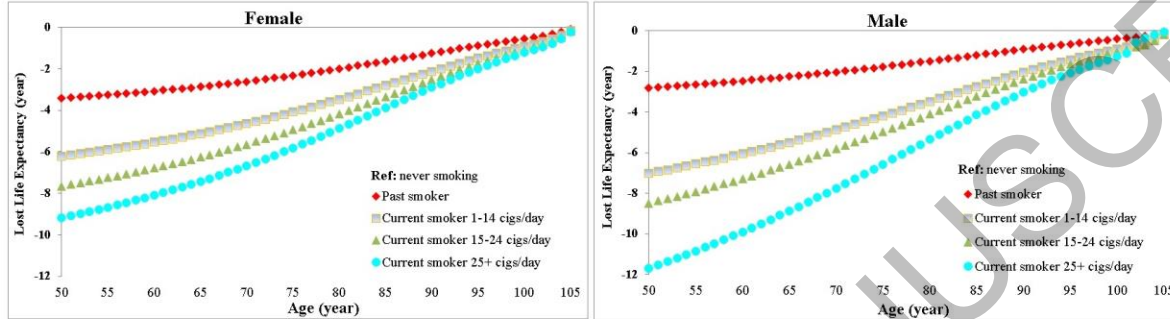


Figure 2

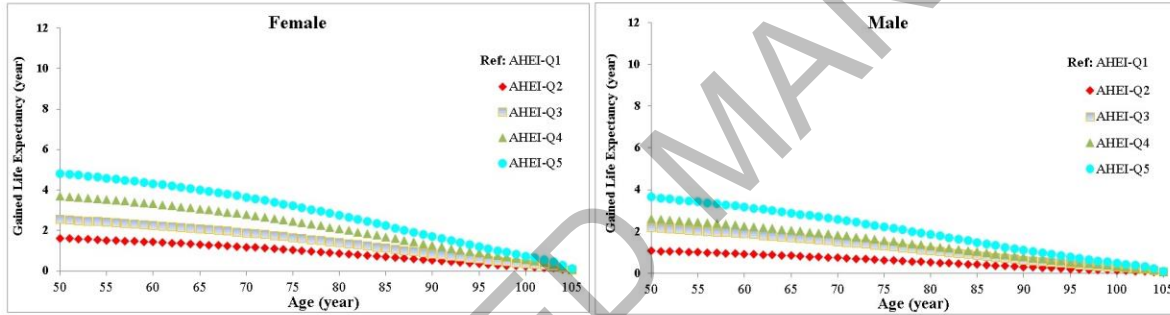
A: Gained life expectancy by increasing physical activity levels as compared to the most sedentary group



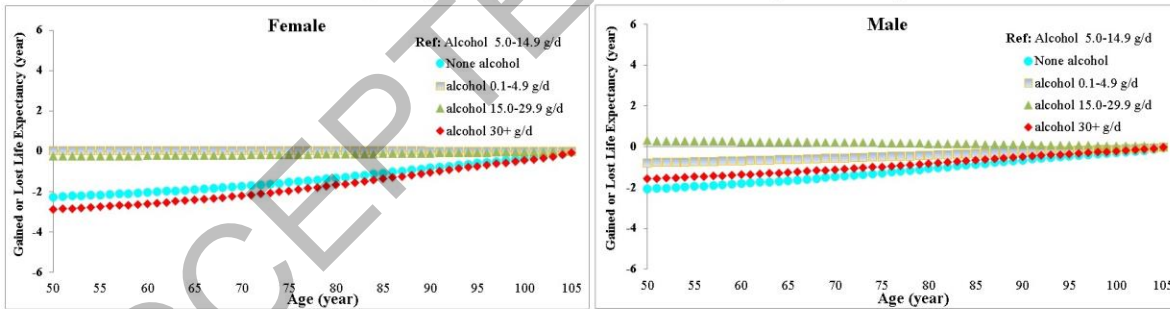
B: Lost of life expectancy due to smoking as compared to never smokers



C: Gained life expectancy by improving diet quality as compared to the lowest quintile of AHEI



D: Gained or lost life expectancy as compared to moderate alcohol consumption (5.0-14.9 g/d)



E: Lost life expectancy as compared with BMI 23-24.9 kg/m²

